

REMARKS

Upon entry of the present amendment, claims 7-13 will be amended, and claims 16-27 will be added, whereby claims 7-14 and 16-27 will be pending.

Support for the amendments to the claims appears in the originally filed specification, at page 7, first full paragraph wherein it is disclosed that, "...fluorocarbon resin molded products such as expanded polytetra-fluoroethylene (ePTFE) or silicides such as silicon can be used."

Moreover, it is noted that an error in the above-noted disclosure has been corrected in the instant amendment by correcting "silicon" to ---silicone---. In this regard, originally filed International Application No. PCT/JP03/11048, of which the present application is the national stage, discloses "silicone".

Accordingly, the present amendment should not be considered to constitute new matter.

Reconsideration of the rejection and allowance of the application in view of the following remarks are respectfully requested.

Response to Art Based Rejections

As previously noted by Applicants in the Amendment filed January 22, 2009 and Reply filed March 23, 2009, which are incorporated by reference herein, the following rejection is set forth in the Final Office Action.

Claims 1 and 4-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,503,527 to Whitmore et al. (hereinafter "Whitmore") in view of Suzuki et al. (hereinafter "Suzuki"), Ionics, Vol. 25, No. 1, pp. 47-54 – with the provided English language translation being referenced by page and line number in the rejection).

In this ground of rejection, it is contended that Whitmore discloses at column 3, line 14, the use of fibrin adhesive composition to anchor dural patches, and that one having ordinary skill in the art would have used the artificial dura material of Suzuki as the dural patch of Whitmore because it exhibits improved cell attachability and thus would be expected to result in a stronger bond with the fibrin glue composition.

The February 3, 2009 Advisory Action asserts that Whitmore explicitly teaches that their fibrin glue may be used to anchor (i.e., adhere) dural patches, with the conclusion that one skilled in the art would have *prima facie* expectation of success in using the fibrin glue to anchor known dural patches, and Suzuki illustrate a prior art dural patch comprising a polymeric material comprising carbon with at least a portion of its surface irradiated with ions. This Advisory Action contends that the adhesive of Whitmore being narrower in scope than the adhesive described by the reference as a whole does not constitute a teaching away from the broader disclosure.

The April 9, 2009 Advisory Action also contends that that Suzuki shows that irradiation alters the ePTFE such that cell attachment appears while no cell attachability is seen with untreated ePTFE, and that one skilled in the art would expect his enhanced attachability to also be exhibited with regard to biological adhesive. This Advisory Action also contends that expected results, if shown, pertain to a particular polymeric material, and are not commensurate in scope with the invention as claimed.

In response to this ground of rejection, Applicants once again note their arguments as previously submitted with the previous response, and incorporate these arguments as if set forth in their entirety herein. Moreover, for the Examiner's convenience in having arguments appearing in one location for review, Applicants are repeating previously

presented arguments while modifying these arguments with respect to the claims as amended herein.

Applicants once again submit that Whitmore relates to a substance which is obtained by chemically immobilizing fibrin-constituting component, such as fibrinogen to hyaluronic acid, chitin or chitosan. Whitmore discloses hyaluronic acid, hyaluronic acid derivative, chitin, chitosan or its derivatives, having an adhesive property with a fibrin glue, and its structure product. Hyaluronic acid, chitin, and chitosan are biologically derived materials. In contrast, the presently claimed subject matter relates to, as recited in Applicants' independent claim 7, a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element, the polymeric material comprising expanded polytetra-fluoroethylene or silicone, comprising irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions to form an ion-modified expanded polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone.

Thus, in Applicants' recited method the fibrin glue is applied to the irradiated at least a portion of the irradiated expanded polytetra-fluoroethylene or silicone to improve affinity of the expanded polytetra-fluoroethylene or silicone. At most, Whitmore discloses the broad anchoring of dural patches. This is a generally known fact that fibrin glue can be usually used in surgery for repair of dura mater. Whitmore is therefore only directed to a conventional surgery method where a fibrin glue is used for prevention of a leak of cerebrospinal fluid in dura mater surgery. Whitmore does not teach or suggest expanded polytetra-fluoroethylene or silicone to which fibrin glue is adhered being formed by irradiation as recited in Applicants' claims.

In particular, Whitmore discloses beginning at column 2, line 45, that his invention relates to a fibrin glue composition comprised of a biocompatible, bioabsorbable hyaluronic acid derivative material, having applied thereto fibrinogen and thrombin. Beginning at column 2, line 62, Whitmore discloses that when placed on a wound site and activated, the compositions of his invention function as a fibrin glue, and that in contrast to conventional fibrin glues, his compositions do not require complex mixing of fibrinogen and thrombin components immediately prior to use and do not require special applicators.

Thus, Whitmore is directed to a fibrin adhesive or sealant composition comprising a biocompatible, bioabsorbable hyaluronic acid material, chitin material, or chitosan material to which fibrogen and a fibrinogen cleaving agent are applied along with other components. It is submitted that one having ordinary skill in the art would not have been motivated to use the disclosed film, or woven or non-woven material of Whitmore with an ion-bombarded polymeric material as recited in Applicants' claims.

Whitmore also discloses uses of his compositions at the top of column 3, wherein it is disclosed that the compositions of his invention can be put to a wide range of suitable medical and surgical uses, and that the compositions can be used in hemostasis applications, as sealants and as adhesives. Moreover, it is disclosed that the compositions of his invention have a number of surgical uses, including, in cardiovascular surgery, they can be used as a hemostatic, for example, with needle holes, suture lines, diffuse and nonspecific bleeding, friable tissue bleeding, aortic dissections, ventricular ruptures, and fistulas. In otorhinolaryngology (ear, nose and throat, ENT) surgery, it is disclosed that they can be used in facial nerve grafts, closure of dural leaks, nasal septal surgeries, and post tonsillectomy hemorrhage. In neurosurgery, it is disclosed that they can be used to

prevent cerebral spinal fluid (CSF) leakage, peripheral nerve repair, and to anchor dural patches. In plastic surgery, it is disclosed that they can be used in a number of procedures relating to skin grafts, including to fix grafts, control oozing and control bleeding. In thoracic surgery, they can be used, for example, in the treatment of pneumothorax and pulmonary leaks. The compounds of Whitmore's invention are also disclosed to have a number of other surgical uses, including, sealing biopsy needle tracks, liver and splenic lacerations, lymphatic fluid leaks, organ resectioning, seroma and hematoma prevention, and gastrointestinal bleeding. Whitmore also discloses that his compositions can be used as a local delivery vehicle for the delivery antibiotics or other biologically active substances to the application site. Whitmore also discloses that his compositions may serve as a surgical adhesion barrier, and that other uses are known in the art or will be apparent to the skilled artisan.

Thus, as the rejection realizes, amongst a multitude of uses, Whitmore broadly discloses use of a dural patch, but does not disclose a dural patch as recited in Applicants' claims. In this regard, as noted above, Applicants' independent claim 7 is directed to a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element, the polymeric material comprising expanded polytetra-fluoroethylene or silicone, comprising irradiating at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone with ions to form an ion-modified expanded polytetra-fluoroethylene or silicone; and applying the fibrin glue to the irradiated at least a portion of a surface of the expanded polytetra-fluoroethylene or silicone.

In an attempt to overcome this deficiency of Whitmore, the rejection relies upon Suzuki (which includes as an author Yoshiaki Suzuki who is one of the inventors of the presently claimed subject matter). However, one having ordinary skill in the art would not

have combined these diverse disclosures. Suzuki discloses that cells are adhered to a polymer which was irradiated with ion beam, and its adhesion strength is improved by irradiation of the ion beam. As disclosed, in Suzuki, such as beginning at page 7, 2.3 Cell culturing method, the cells are cultured *in vitro*, and the cells are selectively adhered to the polymer which was irradiated with the ion beam. In such an "*in vitro*" experiment of cell culturing, the culture solution which contains cells does not contain fibrinogen. The culture solution contains amino acid and serum, which is plasma where fibrinogen is removed. From the results of the *in vitro* experiment of Suzuki, one having ordinary skill in the art would not be capable of predicting that fibrinogen, which is one component of fibrin glue, is adsorbed to a polymer which was irradiated with an ion beam.

Applicants note that the main component of serum is albumin (45%). Based upon the disclosures, even if for the sake of argument the documents were combined, adsorption of albumin may be predicted, but adsorption of fibrinogen would not be predicted. In this regard, prediction based upon an experiment in the absence of fibrinogen is without any support as to any expectation of results with fibrinogen.

Thus, Suzuki discloses that cells are adhered to a polymer which was irradiated with ion beam, and adhesion strength of the polymer is improved by irradiation of ion beam. However, Suzuki does not teach that the adsorption of fibrinogen which is a plasma protein is increased. One having ordinary skill in the art would not be able to predict that the adsorption of fibrinogen is increased in the case of using ion beam-irradiated ePTFE. If it is predicted from Suzuki that the adsorption of fibrinogen is increased by irradiating ePTFE with ion beam, then the adsorption amount of all proteins would be increased. However, this is not a fact. In the cell culturing of Suzuki, the culture solution contains a serum (where fibrinogen was removed). Therefore, it may be

considered that adsorption amount of fibronectin or vitronectin which is involved in cell adhesion is increased, but the adsorption amount of proteins which are not present therein cannot be predicted. The proteins include both proteins which promote cell adhesion and proteins which inhibit cell adhesion. Thus, there is the possibility that the adsorption amount of proteins which inhibit cell adhesion will be increased.

Still further, the Examiner is reminded that independent claim 7 is directed to a method for improving affinity with a fibrin glue of a polymeric material comprising carbon or silicon as a constitutional element wherein the polymeric material comprises expanded polytetra-fluoroethylene or silicone. This is different from repairing body tissue by using an ion beam-irradiated polymeric material. **A review of Applicants' originally filed application, including the Examples reveals that it is unexpected that the adhesiveness between ePTFE and a fibrin glue was remarkably improved in the case of ion beam-irradiated ePTFE as compared with the case of untreated ePTFE (Figs 1 and 2).**

Still further, Applicants submit herewith a copy of Kobayashi et al., Surface & Coatings Technology 201 (2007) 8039-8042 accompanied by a Form PTO-1449 listing this document. The Examiner is requested to include an initialed copy of this form with the next communication from the Patent and Trademark Office. A fee should not be necessary for consideration of this document. However, authorization is hereby provided to charge any required fee for consideration of this document to Deposit Account No. 19-0089.

A review of this document should reveal that it is unexpected that the adhesiveness between silicone sheets and a fibrin glue is remarkably improved in the case of ion beam-irradiated silicone sheets as compared with untreated silicone

sheets. For example, attention is directed to Kobayashi et al., page 8042, Fig.7 and its discussion in the paragraph beginning at the bottom of the right-hand column.

For the reasons set forth above, the advantageous effect of the present invention (improvement of the adhesiveness between ePTFE or silicone, and a fibrin glue cannot be predicted from Whitmore and Suzuki.

Accordingly, Applicants submit that the one having ordinary skill in the art would not have arrived at the subject matter recited in Applicants' claims and/or the results as disclosed and claimed by Applicants. Moreover, Applicants submit that the results shown herein should be considered to be commensurate with the claimed subject matter

Based on the above, it is respectfully submitted that this application is in condition for allowance, the rejection should be withdrawn, and the pending claims, including claims 7-14 and newly-added claims 16-27, and the mailing of a Notice of Allowance is respectfully requested.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the objection and rejections of record, and allow each of the pending claims.

Applicants therefore respectfully request that an early indication of allowance of the application be indicated by the mailing of the Notices of Allowance and Allowability.

Should the Examiner have any questions regarding this application, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
Yoshiaki SUZUKI et al.



Bruce H. Bernstein
Reg. No. 29,027

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GREENBLUM & BERNSTEIN, P.L.C.
1950 Roland Clarke Place
Reston, VA 20191
(703) 716-1191

Arnold Turk
Reg. No. 33094